Tartanised Plasma Exchange Replacement Fluid – Implementing Change Through Crisis Management

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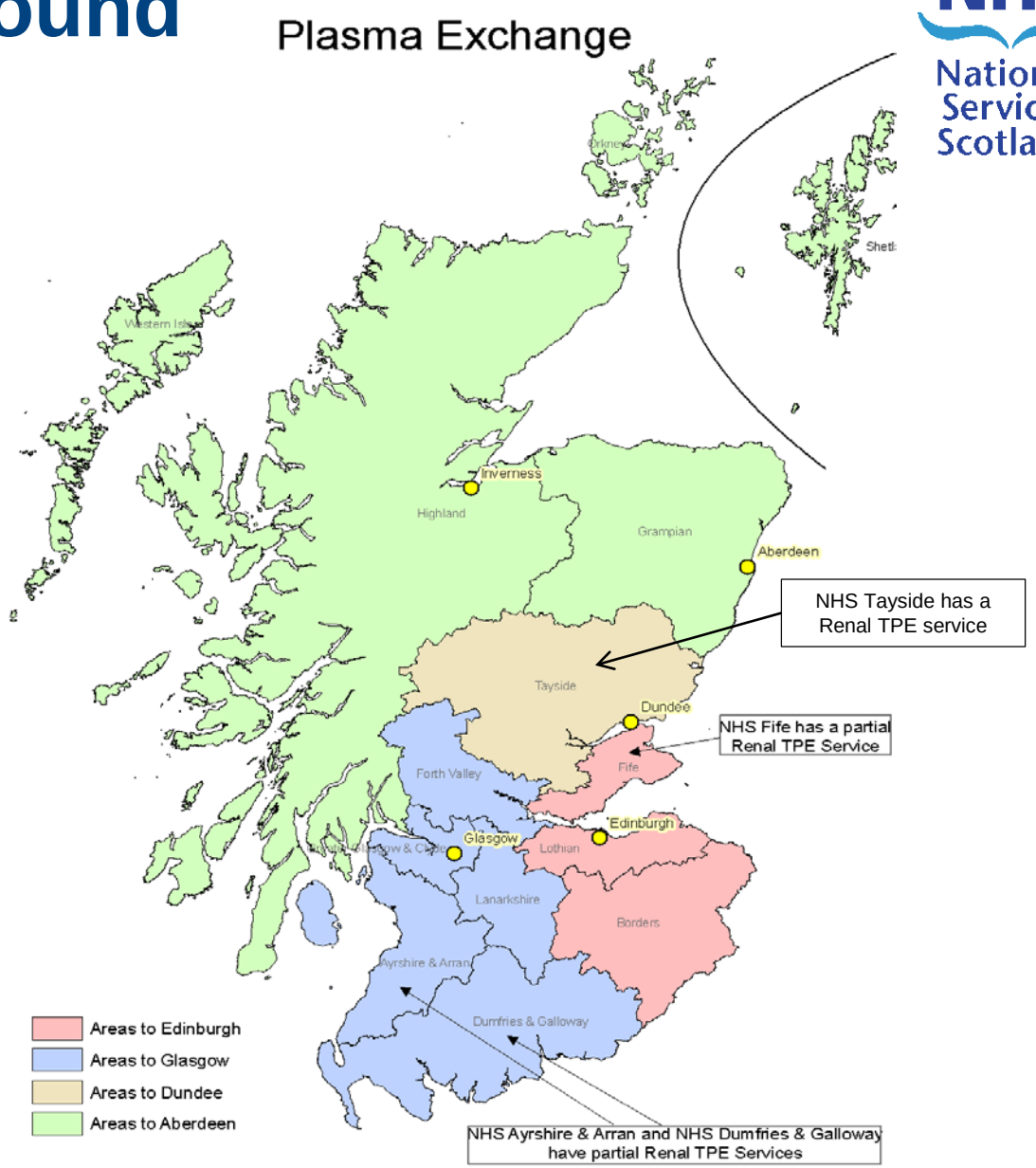
BBTS Glasgow September 2017

Aims

- Set the scene
- Share the experience
- What happened next: 6 month review
- Present-day position:
  - local
  - international
- Lessons learned
- Open to the floor

Background

- TA services: 1 of 4 national themed clinical services
- All PBSC (and related) activity
- > 95% PEX activity
- Tailored regional service repertoire



Background: Activity & Adverse Events

Activity: 2012 - 2013	
PEX	1379
PBSC	361
ECP	120

	Procedure	ACI : N (ACIR)		
2012-13		Citrate	CVS	Allergy
	All TPE PBSC	145 (0.07) 82 (0.06) 60 (0.17)	97 (0.05) 62 (0.05) 25 (0.007)	13 (<0.01) 11 (<0.01) 0
	All			
	Mild Moderate Severe	122 (0.06) 18 (0.01) 5 (<0.01)	54 (0.03) 43 (0.02) 0	9 (<0.01) 2 (<0.01) 2 (<0.01)

- Standard replacement fluid: 4.5 / 5% albumin
- 2008: National Plasma Product Expert Advisory Group : NPPEAG

Sharing the Experience: 14th August 2013...

Sharing the Experience: Driver to Change

12th August 2013

Dear Colleague

Supplies of 5% Human Albumin for infusion (500mls)

Currently NHS Scotland has a framework contract for the supply of 5% Albumin. Most unfortunately the number 1 supplier on the framework contract has advised us of a supply chain issue and is not able to supply us the required level of Albumin. The number 2 supplier has no extra stock to give us and is currently on a planned 3 week shut down. We have managed to secure a delivery of 1500 vials, off contract from another supplier but that is all they have available. This means we currently have only 1 month's stock to do us until the end of October unless we are successful in getting further product from another supplier. This difficulty involves the whole of the UK and so we are competing nationally to purchase further product.

Wherever possible, can alternatives to albumin be used to try and safeguard stocks.

Yours sincerely

Dr Rachel Green
(on behalf of the National Plasma Product Expert Advisory Group (NPPEAG))
Consultant in Transfusion Medicine (SNBTS)

Sharing the Experience: Options...

Do nothing	On-going demand	Not an option
Alternative provider	Transfer of issue	Not an option
Alternative fluids	saline plasma starch gelofusine	Explore

Sharing the Experience: Driver to Change – Patient Safety

NHS National Services Scotland

Alternatives

- saline — ✗ used elsewhere; hypotension
- plasma — ✗ used in 1970s; unnecessary donor exposure
- starch — ✗ MHRA licensing withdrawal June 2013
- gelofusine — ✓ blood filled with albumin concern over allergy

Risk Assessment and Mitigation

- Pro-actively seek atopy / allergy history

The *allergic response rates* reported are *low*, with reported allergic responses occurring in between *0.001 – 0.146%* of patients. *Males* and those *with a history of atopy* (previous allergic responses, or history of asthma, hay fever, eczema etc) seem to be more likely to experience an allergic-type response, and so staff should take an allergy history from patients prior to commencing procedures. If a history of allergy is obtained or the patient is male, staff should still undertake the procedure, and monitor the patient closely. **If there is a past history of allergy to gelofusine, this product must <u>not</u> be used, and the exchange must be carried out using 5% albumin only.**

- Capture all adverse events

3. Continue to record all suspected or definite adverse reactions during procedures.

Rapid Implementation

- Operational Action Plan
  - 50:50 mix 5% albumin: gelofusine
  - Start with 5% albumin
  - Preserve 5% albumin - use entire bottle, or none of the final bottle: apply clinical judgement
  - Implementation dependent upon local pharmacy procurement of gelofusine
  - Continue to use plasma wholly or partially, where indicated
  - Use for 6 months then review while continuing to use mix

So What Happened?
June 2014

Evaluation to determine potential for on-going use of the 50:50 mix:

- cost implications
- safety profile

- these factors were evaluated over the initial 6 month usage period (September 2013 – February 2014) and findings compared with the same period in the preceding year (ie September 2012 – February 2013).

Evaluation : June 2014

In scope

- PEX procedures Aberdeen, Edinburgh & Glasgow
  1st September 2013 – 28th February 2014

Findings

- 524 procedures carried out (v 596 2012- 2013)
- 1482 x 500 ml albumin
- 1329 x 500 ml gelofusine
- Where actual amount of replacement fluid was not recorded, use of 50:50 mix was assumed
- Assumed a greater number of albumin bottles was used if an odd number of bags and bottles was recorded (ie first fluid used was albumin).

Safety first...

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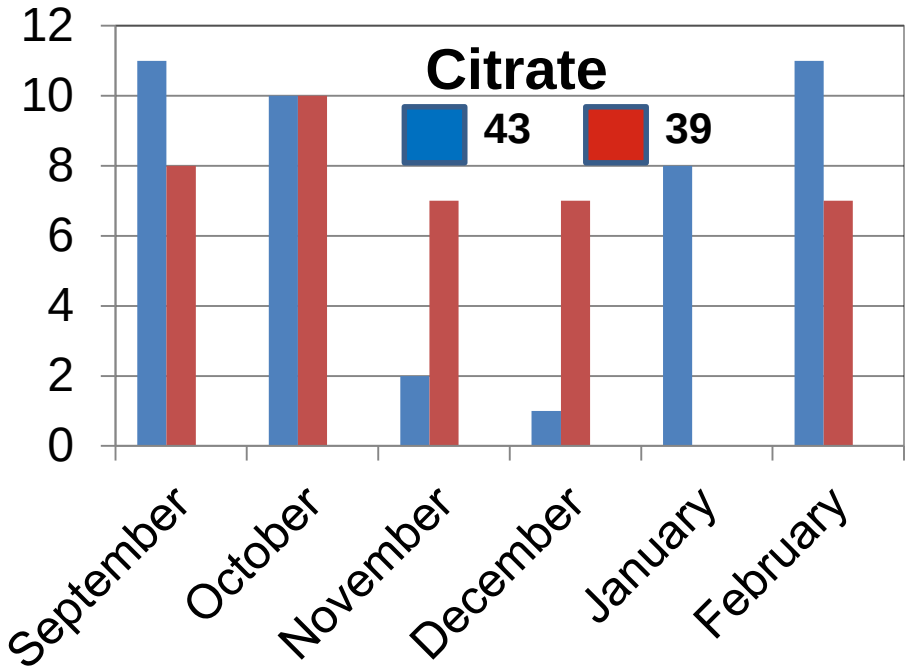
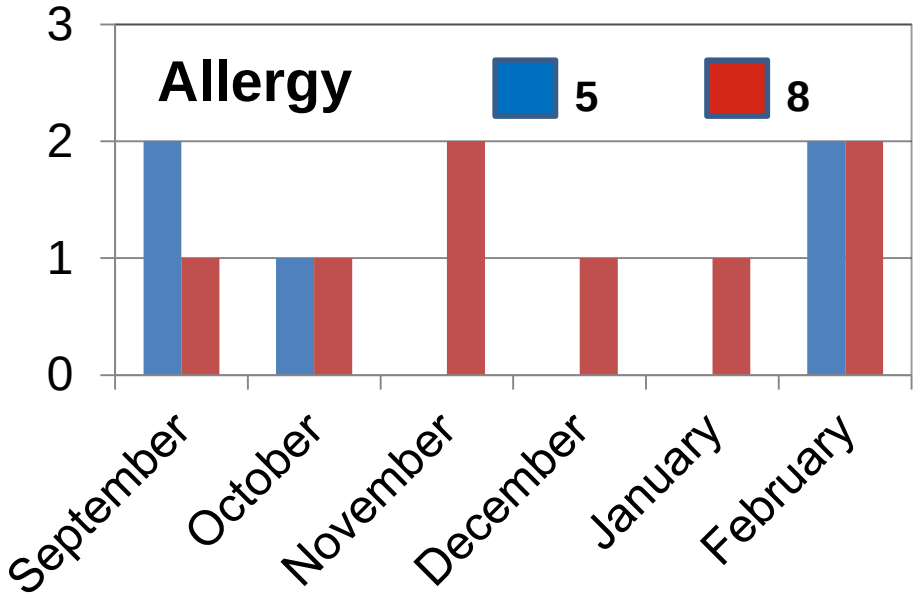
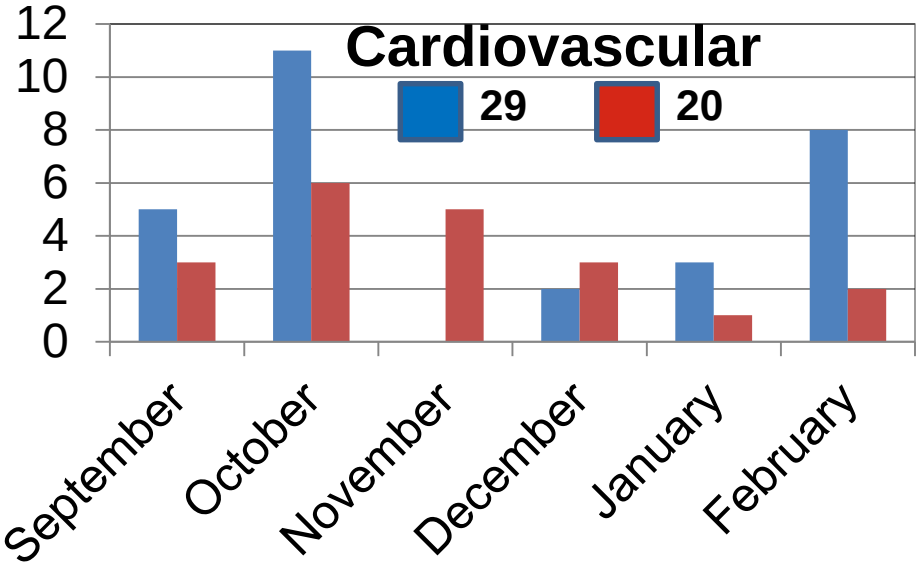


2012/13

2013/14





Severity of TPE Adverse Events : All Centres

2012/13	Citrate			CVS			Allergy		
	mild	mod	severe	mild	mod	severe	mild	mod	severe
Sept	9	2			5		1	1	
Oct	7	3		6	5				1
Nov	2								
Dec	1				2				
Jan	8			1	2				
Feb	11			7	1		1		1
Total	38	5	0	14	15	0	2	1	2
2013/14	mild	mod	severe	mild	mod	severe	mild	mod	severe
Sept	8			1	2			1	
Oct	8	2		3	3		1		
Nov	6	1			5		1		1
Dec	5	2			3		1		
Jan	6				1				1
Feb		1				2	1		1
Total	33	6	0	4	14	2	4	1	3

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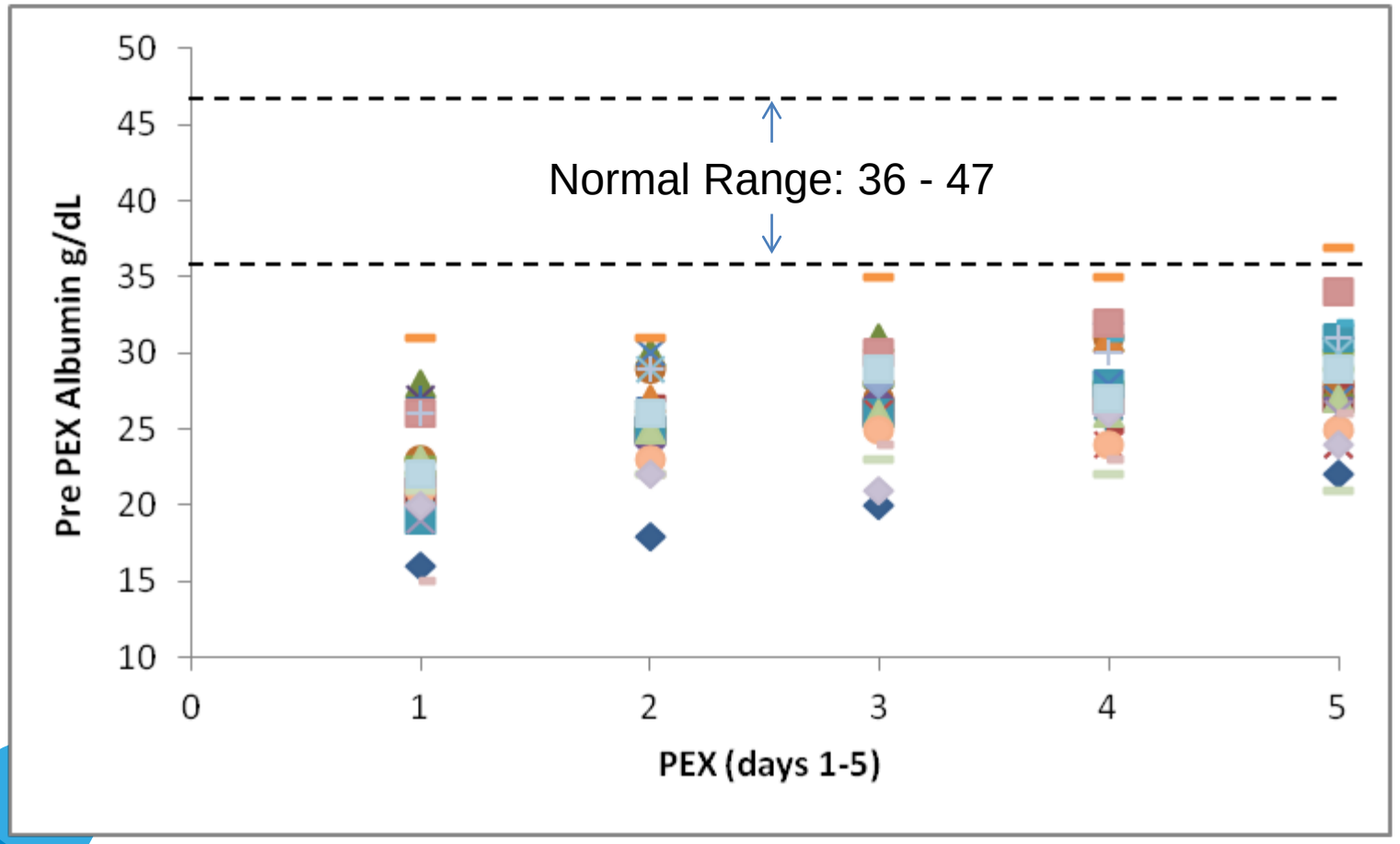
Safety First...
Pre-TPE Albumin



Retrospective analysis - 30 patients 2014 - 2017

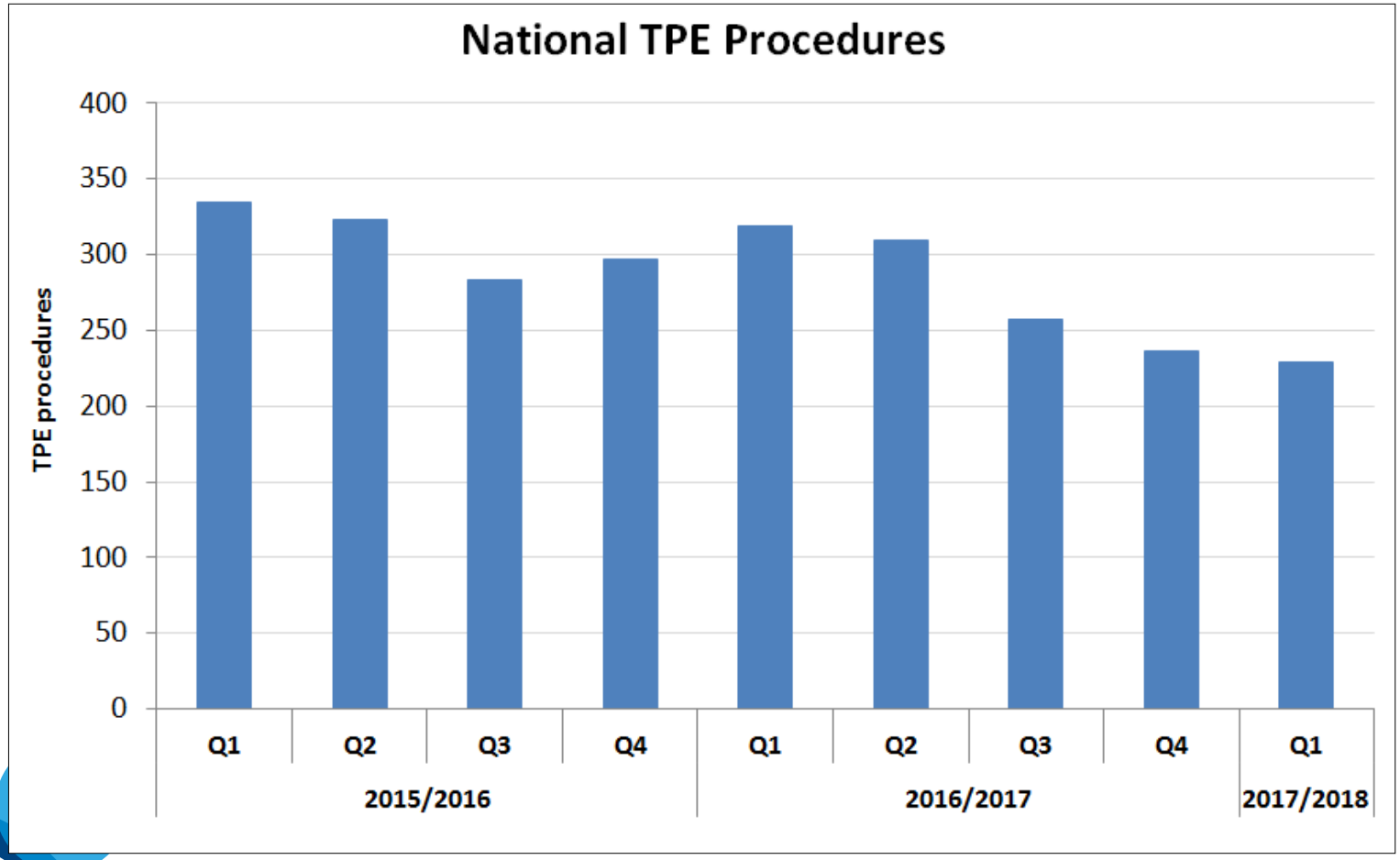
Evaluation : June 2014

Financial Impact

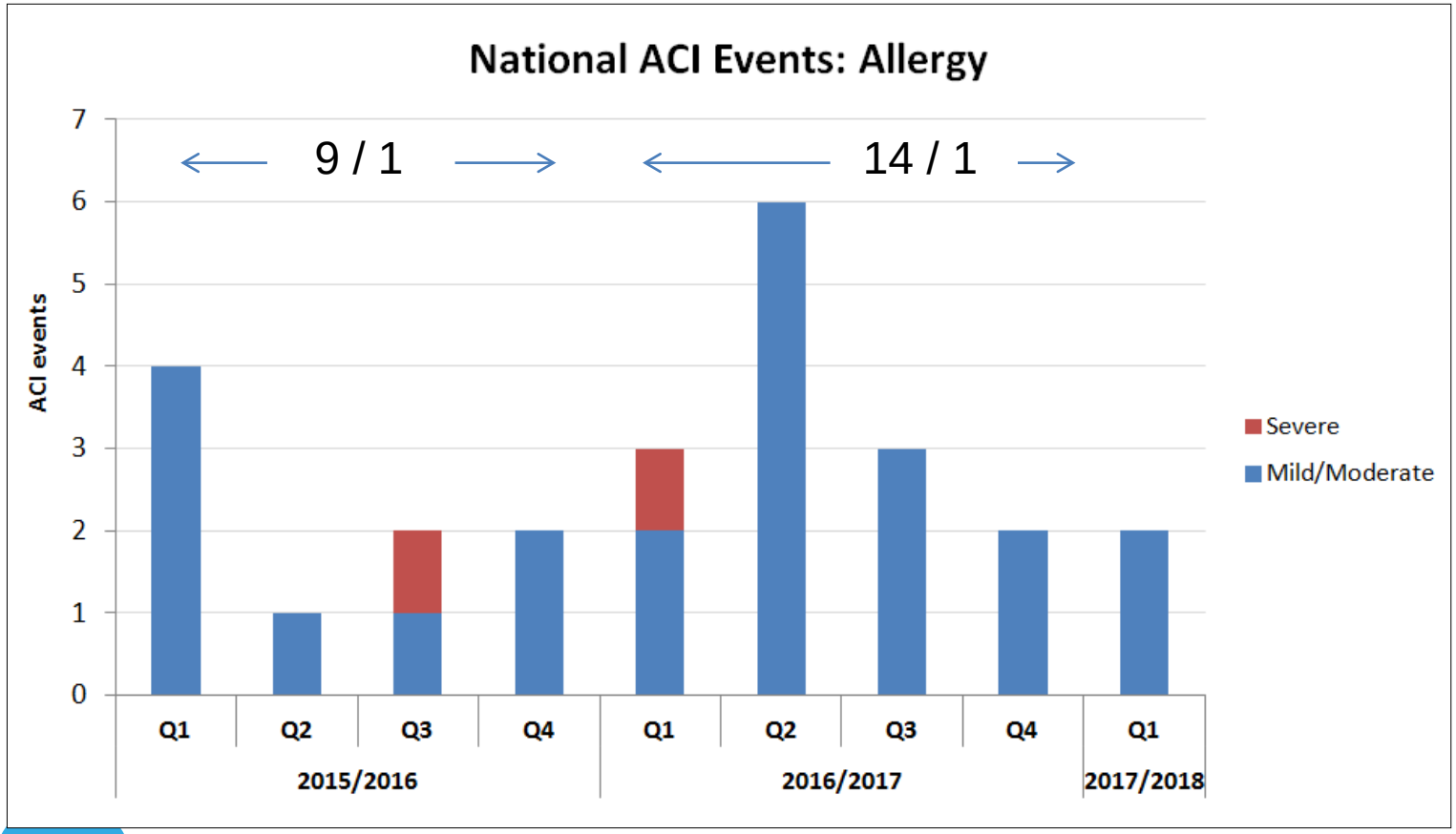
- Costings based on unit cost of £35.05 for albumin and £2.11 for gelofusine

PEX Fluid Replacement Costs 1st September 2013 – 28th February 2014	**£**
Total cost of 5% albumin	51944
Total cost of gelofusine	2804
Total cost of 5% albumin / gelofusine	54748
Predicted cost if 5% albumin alone had been used	98525
6 month saving using 50:50 albumin:gelofusine mix v 5% albumin alone	£43777
	(44% saving)

Present Day : Our Practice



Present Day : Our Practice



Present Day : Our Practice

‘Guesstimated’ Savings for NHS Scotland Since 1st September 2013 Using 50:50 mix as Standard PEX Replacement Fluid	
Assume 1000 TPE per annum	
Assume 3L PV removal per TPE	
Assume 1.5L use of 5% albumin and of gelofusine per TPE	
Cost saving per annum	£98,820
Cost saving Sept 2013 – Aug 2017 (47% saving)	£395,280

Present Day : Practice Elsewhere

Journal of Clinical Apheresis 7:124–125 (1992)

Short Report

Succinylated Gelatin as Partial Fluid Replacement in Chronic Therapeutic Plasma Exchange

Sue Gregor-MacGregor and Charles D. Pusey

Renal Unit, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London, England

- 7 patients underwent 285 PEX over 15 months.
- Prospective study.
- Weekly – monthly regimens.
- Rx: 500ml gelofusine in 3L PEX or 1000ml gelofusine in 4L PEX
- Findings: no adverse reactions, no changes in PT, albumin.
- Cost saving: £6/L gelofusine v £90 / L albumin

Present Day : Practice Elsewhere

NHS National Services Scotland

Winning Combinations....

- **Le Conte et al 1997. Inten Care Med 23(3):343-4**
  Replacement Fluids in Plasmapheresis: Cross-Over Comparative Study
  - 4% albumin v 4% albumin+dextran v 4% albumin+HES
  - good haemodynamic tolerance
  - reduced [protein] albumin+HES < albumin+dextran<albumin
  - 25-30% colloid + albumin mix clinically well tolerated
  - 12% cost reduction

- Smithyman 2003, 2006: UCHL Plasma Exchange: Introduction and Guidelines
  - 2.5L colloid + 2U FFP
  - crystalloid 20-40% volume + colloid

- **Ping et al 2015. J Clin Aph 30(2):77-78**.
  Using Normal Saline as Part of Replacement Fluid in TPE
  - 1L NS+2L 5% albumin v 3L 5% albumin
  - no difference in hypotensive rate between groups
  - $5K saving

Present Day : Practice Elsewhere

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Safety First...

- Summary of Product Characteristics

- Succinlylated gelatin (4% W/V solution for infusion)
  - 4.4
    - i) severe anaphylaxis or anaphylactoid reactions have been reported following intravenous administration.....

      These are rare, having an incidence of between 1 in 6,000 and 1 in 13,000 units (0.017 – 0.008%).

      .....may be more likely .....if given rapidly to normovolaemic patients, and may be assumed to be more hazardous in patients with known allergic conditions such as asthma.

Present Day : Practice Elsewhere

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Safety First...

- **Ring et al 1977. Lancet 1: 466-469**.
  - Incidence and severity of anaphylactoid reactions to colloid volume substitutes.
  - 200,906 infusions, 69 anaphylactoid reactions(0.033%)
  - ***Gelatin solutions***: 0.115% incidence; severe reactions 0.038%

- **Milton et al 1984.Clin Haematol 13:75-92**.
  - Synthetic plasma volume expanders – their pharmacology, safety and clinical efficacy
  - 0.066-0.146% anaphylaxis incidence
  - more common in males, with atopy, and early onset

Present Day : Practice Elsewhere

NHS National Services Scotland

Safety First...

- **Laxenaire 1994. An FR Anesth Reanim 13(3):301-10**
  Anaphylactiod Reactions to Colloid Plasma Substitutes: Incidence, Risk Factors, Mechanisms. A French Multicenter Prospective Study.

  - 19,593 patients; 1 of 4 colloids - 48.1% gelatin
  - Overall, 43 analphyactoid reactions (0.219%)
  - Specifically, 0.345% gelatins v 0.099% albumin (RR albumin 3.4x less v gelatin)
  - Independent risk factors: drug allergy, being male

Present Day : Practice Elsewhere

Journal of Critical Care 35 (2016) 75–83

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

How safe is gelatin? A systematic review and meta-analysis of gelatin-containing plasma expanders vs crystalloids and albumin☆,☆☆,★

Claudia Moeller [a,1], Carolin Fleischmann [a,b,1], Daniel Thomas-Rueddel [a,b], Vlasislav Vlasakov [a], Bram Rochwerg [c], Philip Theurer [a], Luciano Gattinoni [d], Konrad Reinhart [a,b,*], Christiane S. Hartog

- 3,629 patients over 1976 - 2012
- 30 RCTs, 8 non-randomised studies, 22 animal studies.
- RCTs: 20 in surgical patients, 7 paediatrics.
- Pharmacovigilance database 1982 - 2014: 239 reports
  local allergy (149), resp dysfunction (105),CVS dysfunction (129)

Conclusions: gelofusine may have adverse effects
significantly increased risk of anaphylaxis (3-fold)
but low certainty of evidence
(RR 3.01, 95% confidence intervals1.27-7.14)

Reflections

- Don’t leave til you leave ⟹ once you’ve left, you’ve left.....close the door and leave the building

- Drivers to change: resilience building during adequacy
  - ‘the ability to survive a crisis and thrive in a world of uncertainty’

- Team work and effective communication are crucial when implementing (rapid) change

- a critical pillar of change: patient safety
  - risk assessment
  - risk mitigation
  - proportionality

In Summary

TRANSFUSION MEDICINE
Official Journal of the British Blood Transfusion Society
British Blood Transfusion Society
Transfusion Medicine | GUIDELINES

Guideline on the clinical use of apheresis procedures for the treatment of patients and collection of cellular therapy products

C. Howell,[1] K. Douglas,[2,3] G. Cho,[4] K. El-Ghariani,[5] P. Taylor,[6] D. Potok,[7] T. Rintala[8] & S. Watkins[9]

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Received 12 March 2015; accepted for publication 21 April 2015

Use of a 50:50 mix of 5% albumin:gelofusine as the replacement fluid for plasma exchange (outwith thrombotic thrombocytopenic purpura cases) is ***cost effective***, ***safe*** and, based on the evidence available, ***clinically effective***.

Use of this fluid combination as the standard replacement fluid for plasma exchange (with the exceptions, above) is consistent with the 2015 BCSH guideline on the clinical use of apheresis procedures.

Thanks To....

- Ioannis Koutsavlis
- June Fotheringham and Kate Forrester

- SNBTS TA theme members